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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/896,962	06/29/2001	George B. Sigal	100405-6205	1824

7590

07/03/2002

Barry Evans, Esq.
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New York, NY 10022

EXAMINER

MAUPIN, CHRISTINE L

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 07/03/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/896,962

Applicant(s)

SIGAL ET AL.

Examiner

Christine L. Maupin

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 78-99 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 78-99 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of the invention of group I drawn to a microparticle comprising a core and electrochemiluminescent moieties in Paper No. 6 is acknowledged. Applicant's election with traverse of restriction in Paper No. 6 is acknowledged. The traversal is on the ground(s) that the search of the inventions of groups II and I would not be burdensome, because the search of microparticle would encompass a search of methods using the microparticle. This is not found persuasive because the separate classification of the two groups is *prima facie* evidence of the burden of examination, which is not rebutted. Therefore the restriction is maintained. The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claim 98 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

After carefully considering the conditions for the applicant's request of receiving the benefit of an earlier filing date of October 5th 1995, application 08/437,348 issued patent No. 5,679,519. The applicant's claim for domestic priority under 35 U.S.C. 120 is denied. The patented application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 120 for all pending claims 78-97 and 99 of the instant application and the instant application has no inventor/inventive entity in common and the October 5th 1995; application 08/437,348 issued patent No. 5,679,519. See MPEP § 201.07.

Further, after carefully considering the conditions for the applicant's request of receiving the benefit of an earlier filing date of 20th 1997, application 08/954,355 issued patent No.

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5,096,500. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant is reminded of the proper content of an Abstract of the Disclosure.

In chemical patent abstracts for compounds or compositions, the general nature of the compound or composition should be given as well as its use, e.g., "The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics." Exemplification of a species could be illustrative of members of the class. For processes, the type reaction, reagents and process conditions should be stated, generally illustrated by a single example unless variations are necessary.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 78-97 and 99 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

All of these claims encompass cores and electrochemiluminescent compounds where the electrochemiluminescent moieties are "Within said core". The dependent claims specifically identify a few particular core materials such as plastic, carbon, fullerenes and metals such as gold. The claims also encompass electrochemiluminescent moieties such as Ruthenium or Osmium, but the specification only exemplifies the use of cores of colloidal gold, silica and titanium oxide. There is no example in the specification in which an ECL reagent is "within said core".

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that:

" A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers*, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

It is noted that in *Fiers v. Sugano* (25 USPQ2d, 1601), the Fed. Cir. concluded that

"...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

In the application at the time of filing, there is no record or description, which would demonstrate conception of any microparticle, which has an ECL reagent "within said core". That is, there is no description other than in the claim, which permits an ordinary practitioner to determine what species would function, how they would function or how such a core containing ECL reagents would be synthesized. Therefore, the claims fail to meet the written description requirement by encompassing species, which are not described in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 78-97, and 99 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is vague and indefinite what is meant by the term "core". It is unclear what are the metes and bounds of the term "core". Hence the core, for purposes of the 102(b) rejections is interpreted as the center element of the complex.

It is vague and indefinite what is meant by the phrase "within said core". It is unclear if this requires simple attachment of the ECL reagent to the core or if it actually requires formation of doped core which contains, for example, a mixture of Ruthenium and Gold. No such doped core is exemplified by the specification and consequently, the written description rejection is made based upon this interpretation.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 78, 85, 86, 87, 88, 94, 95, 96, 97, are rejected under 35 U.S.C. 102(b) as being anticipated by Blackburn et al., Clin. Chem., Vol. 37, No. 9 (1991), pp 1534-1539. Here Blackburn teaches a electrochemiluminescence microparticle with;

1) a metal core, here Ruthenium (II) is the metal core (page 1534, column 2);

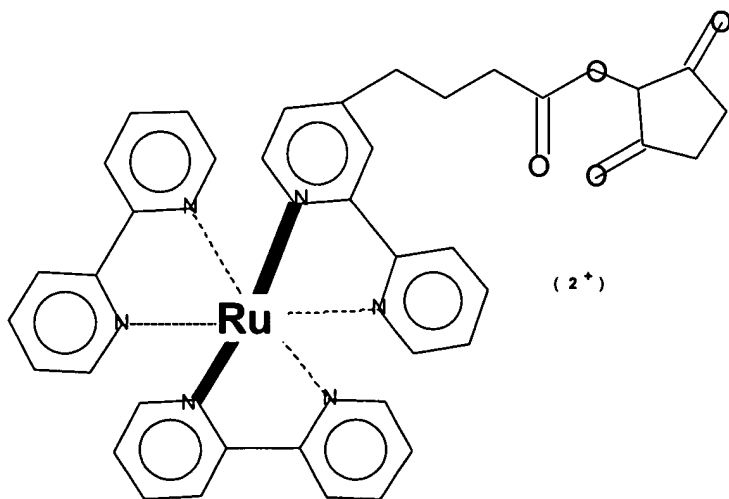
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2) a metal core being a transition metal, here Ruthenium (II) is the metal core (page 1534, column 2);

3) electrochemiluminescent moieties, here the bipyridyl groups attached, to form the microparticle Ruthenium (II) tris(bipyridyl) $\text{Ru}(\text{bpy})_3^{2+}$ (page 1534, column 2);

4) having a co eactant binding reagent that will attached to tripropylamine (TPA), proteins, haptens, antibodies(page 1536, column 1, second paragraph) and nucleic acids readily. In this instant the complex that was used was $\text{Ru}(\text{bpy})_3^{2+}$ here the label is an NHS ester shown below (page 1534, column 2);

5) the core is electrically conductive, here Blackburn shows the core is conductive with a gold electrode(page 1535, figure 1 and caption).



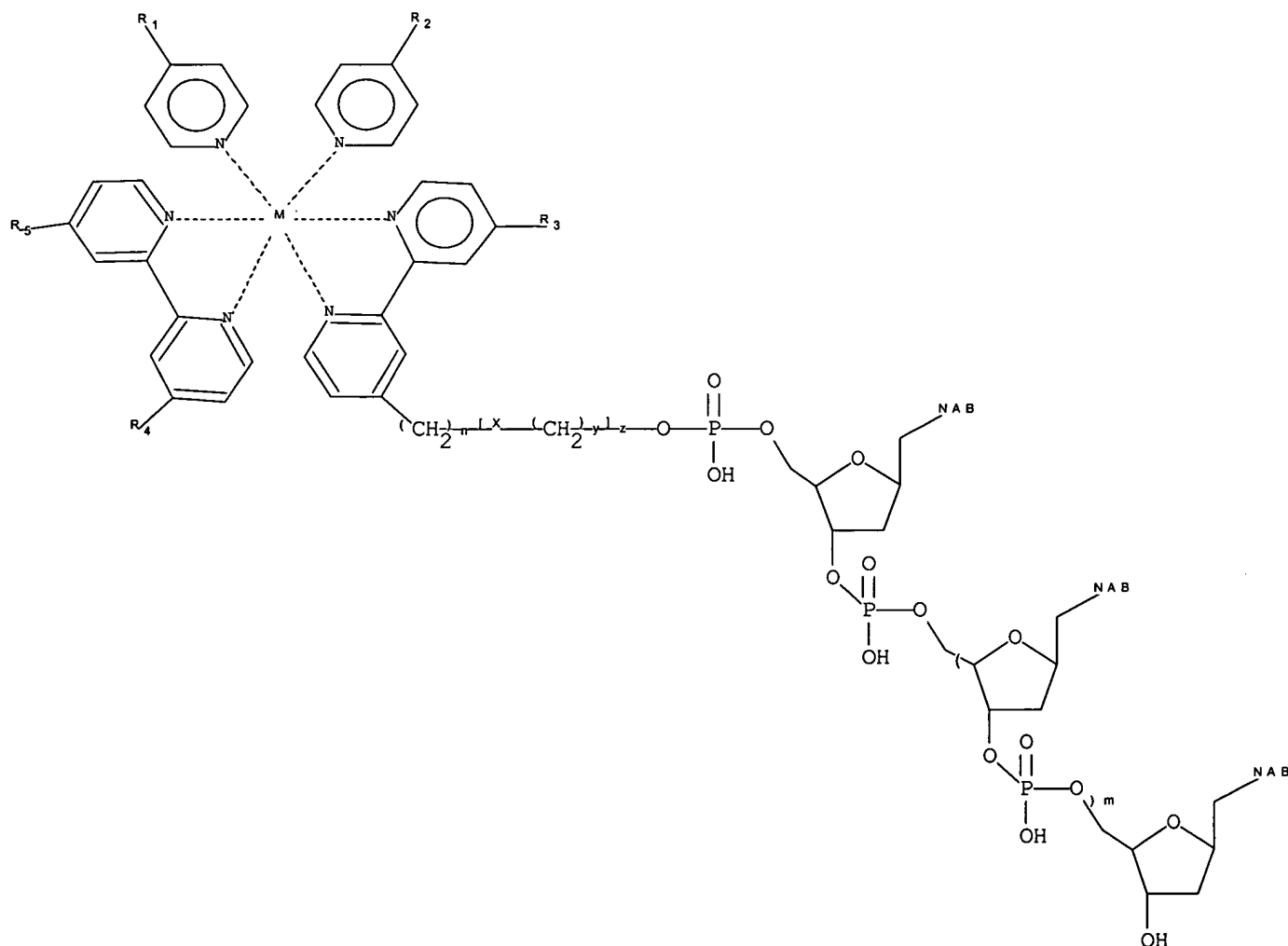
Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 78, 85, 86, 87, 88, 94, 95, 96, 97, are rejected under 35 U.S.C. 102(b) as being anticipated by Gudibande et al., US patent No. 5,597,910, issued 28th of January 1997. Here, Gudibande teaches an electrochemiluminescent particle with a metal center that will attach to

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oligonucleotides using phosphoramidite chemistry (abstract, and column 6, lines 41-42, and column 40-42). Gudibande states, "that electroluminescence labels are those, which become luminescent species when acted on electrochemically. They provide a sensitive and precise measurement of the presence and concentration of an analyte of interest. In such techniques, the sample is exposed to a voltammetric-working electrode in order to trigger luminescence. The light produced is measured and indicates the presence or quantity of the analyte". (column 9, lines 11-17) Gudibande discloses the electrochemiluminescent particle:



Here the variables may be:

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a) M may be Ru, Re, or OS (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

b) R_1 , R_2 , R_3 , R_4 , and R_5 are the same or different and each is H or alkyl of 1-4 carbon atoms; (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

c) n is an integer from 1-20, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

d) X is selected from the group consisting of O, S, SO_2 , COO, CONH, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

e) y is an integer of from 1 to 20, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

f) z is an integer from 1 to 1000, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

g) NAB is a nucleic acid base which may be modified or unmodified; said complex being able to electrochemiluminescence, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

h) the nucleic acid is a primer for a polymerase amplification, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42);

i) the nucleic acid is a hybridization probe, (column 9, lines 50-68, column 10 lines, 1-43, and columns 41-42).

Here Gudibande et al., teaches an electrochemiluminescence microparticle with;

1) a metal core, here M may be Ru, Re, or OS may be the metal core (column 9, lines 50-68, column 10 lines, 1-43);

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2) a metal core being a transition metal, here M may be Ru, Re, or OS may be the metal core (column 9, lines 50-68, column 10 lines, 1-43);

3) electrochemiluminescent moieties, here the bipyridyl groups, to form the microparticle M with ligands such as but not limited to tris(bipyridyl) $M(bpy)_3^{2+}$ (column 9, lines 50-68, column 10 lines, 1-43), with alternate groups such as substituted or unsubstituted phenanthroline groups (see structures in columns 9-12)

4) having a coreactant binding reagent that will attached to nucleic acids readily. In this instant the complex that was used was $M(bpy)_3^{2+}$ or other ligands, here the binder is an phosphoramidite substituted or unsubstituted with the groups consisting of $-N(CH_2CH_2)_2-$, $-NH-CH_2CH_2-$, $-O-CH_2CH_2-CN$, $O-CH_3$, or morpholino provided that neither of the above groups are identical, (column 10 lines 20-36);

5) the core is electrically conductive, here Gudibande shows the core is conductive with a gold electrode that the luminescence is generated by an electrode(column 11, lines 14) and that the relative electrochemiluminescence is substantial when bound to a bio-molecule, (column 13, lines 12).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 83 is rejected under 35 U.S.C. 102(b) as being anticipated by Mandle et al., US patent No. 4,372,745. Here Mandle et al., teach that electrochemiluminescent particles are enclosed with in a liposome. Mandle teaches labeling an immunological species specific to the analyte of interest with a encapsulated fluorescer material which is biologically compatible with

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such species is then contacted with the encapsulated fluorescer labeled species and the biological of interest to form an encapsulated fluorescer labeled specie/biological complex; (column 4, lines 34-39). Further Mandle teaches that by contacting the freed fluorescer with and energy source other than electro magnetic radiation, capable of activating the fluorescent label (column 4, lines 44-46).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 78-82, 84-97, and 99 are rejected under 35 U.S.C. 102(b) as anticipated by Oprandy US Patent No. 5,679,519, issued October 5th 1995. Here, Oprandy teaches an electrochemiluminescence microparticle with regards to claims 78, 79, 82, 86-88, 94-97, and 99;

1) a metal core, here Ruthenium (II) is the metal core (see figure 1 and column 4, lines 66-68);

2) a metal core being a transition metal, here Ruthenium (II) is the metal core (see figure 1 and column 4, lines 66-68);

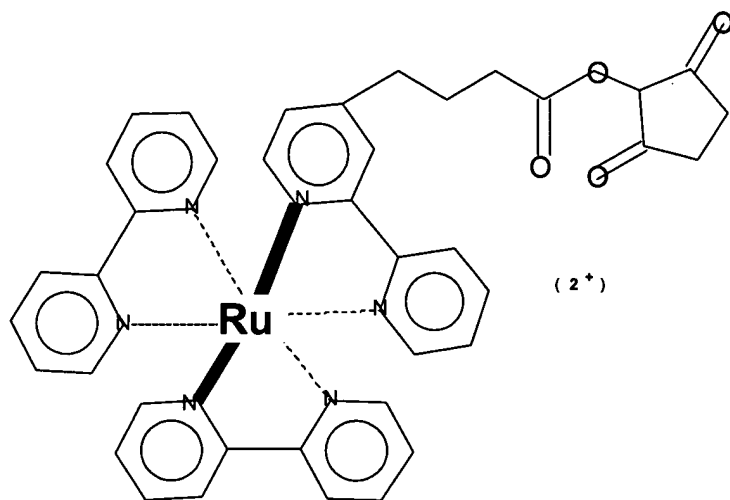
3) electrochemiluminescent moieties, here the bipyridyl groups, to form the microparticle Ruthenium (II) tris(bipyridyl) $\text{Ru}(\text{bpy})_3^{2+}$ (see figure 1 and column 5, lines 1-8);

4) having a coreactant binding reagent that will attached to tripropylamine (TPA), (see figure 1 and column 4, lines 66-68) nucleic acids readily. In this instant the complex that was

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used was $\text{Ru}(\text{bpy})_3^{2+}$ here the label is an NHS ester shown below (see figure 1 and column 5, lines 1-8);

5) the core is electrically conductive, here Oprandy disclosed that the center is oxidized at the surface with a gold or platinum electrode(see figure 1 and column 4, lines 66-68 and column 5, lines 1-8);.



In regards to claims 84-97, and 99, Here Oprandy further expresses that an option to the single metal center or core, a multiple mixed metal, carbon fibrils (column 5, lines 35-36) or magnetic metals or the like may be used in the alternative. Oprandy states that this would include magnetic beads that carry an oligonucleotide probe which serves as the capture probe (column 7, lines 28-30). Oprandy states that the use of beads that are polystyrene microparticles having an iron oxide center would make them super para-magnetic (column 7, lines 35-39). Further coating the bead with another means of affixing the oligonucleotide capture probe would also allow for electrochemiluminescent use (column 7, lines 40-49).

With the use of magnetic cores as opposed to the single metal element of Ru, Re, or Os, Oprandy teaches one of ordinary skill in the art to use mixed metal centers or cores to increase the conductive properties of the complex. This would include using materials that contain sites

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such as pores or relatively large spaces in between molecule in the elemental space groups such as carbons, fullerenes or titanium or polymers to seed or dope with metals that are magnetic or have both magnetic and electrochemiluminescent properties.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 78-82, 85-91, and 94-97, and 99 are rejected under 35 U.S.C. 103(a) as being anticipated by Shah et al., WO90/05301 issued 17 May 1990. Shah teaches a complex comprising a center and electrochemiluminescent moieties within said center, here Shah et al., discloses

In regards to claim 78, Shah teaches a composition that includes a plurality of suspended particles capable of binding to a component assay mixture;(page 5, lines 12-16, abstract), with an electrochemiluminescent moiety that is linked to suspended microparticulate matter;(page 5, lines 26-29, abstract), with a plurality of suspended particles capable of specifically binding with an analyte;(page 6, lines 16-17),

In regards to claims 79-82, here Shah teaches that the microparticulate matter may be crosslinked with starch, dextrans, cellulose, proteins, organic polymers, styrene copolymers, styrene/butadiene copolymer, acrylonitrile/butadiene/styrene copolymers as well as inorganic silicas;(page 14, lines 27-34), Shah further teaches that the preferred embodiment is that the particles are suspended within the electrochemiluminescent system;(page 14, lines 35-36).

In regards to claims 85-91, here Shah teaches that the microparticle metals moieties may be organic metallic compounds such as Re or bipyridine complexes, chelating agents that will luminesce in electrochemical conditions, rare-earth metals, transition metals, preferable Ru, Os, Re, Ir, Rh, Pt, In, Pd, Mo, Tc, Cu, Cr, W, or especially preferred are Ru and Os;(page 11, lines 1-15).

In regards to claims 94-99,here Shah teaches ligand assay binding to surface groups that will covalently bond with the microparticle examples of binding partners are antibodies, enzymes, nucleic acids or protein;(page 6, lines 29-34) and whole cells, surface antigens, subcellular particles, virus, prion, viroid, antigens, haptens, lipids, fatty acids, nucleic acid, polysaccharide, protein, lipoprotein, glycoproteins, peptide, polypeptide and others (see page 10 lines 15-33).

Therefore it would be prima facie obvious to one skilled in the art to make electrochemiluminescent particles that contain mixed metal centers, or plastic centers motivated by Shah teaching that more binding partners may be attached to the moiety or have a plurality of binding species in one particle to make particles with these properties.

Conclusion

All claims are drawn to the same claimed invention (Group I) 78-97 and 99 have been rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine L. Maupin; whose telephone number is (703) 308-3617 and fax number is (703) 746-7641.

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The examiner is normally in the office between the hours of 9:30 a.m. and 5:30 p.m., and telephone calls either in the morning or the mid-afternoon are most likely to find the examiner in the office.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1234.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the U.S.P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 308-4242 or (703) 308-2724. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

July 1, 2002

Christine L. Maupin
Examiner
Art Unit 1637



JEFFREY FREDMAN
PRIMARY EXAMINER